

Attorney Docket No. 3477.89  
Serial No. 09/674,237  
Filed: July 24, 2001  
For: ESE GENES AND PROTEINS  
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AMENDMENTS TO THE CLAIMS:

1. (Currently amended) An isolated nucleic acid comprising a nucleotide sequence ~~encoding a mammalian Ese1 protein or a splice variant thereof selected from the group consisting of:~~

- (a) a nucleotide sequence encoding the amino acid sequence of SEQ ID NO:3;
- (b) SEQ ID NO:1;
- (c) SEQ ID NO:2;
- (d) a nucleotide sequence at least 80% identical to a sequence of (a) to (c);
- (e) a nucleotide sequence at least 90% identical to a sequence of (a) to (c); and
- (f) a nucleotide sequence completely complementary to a sequence of (a) to (e).

2-6. (Canceled)

7. (Currently amended) An isolated nucleic acid comprising a nucleotide sequence of at least 10 consecutive nucleotides selected from the group consisting of ~~Sequence ID No. 1SEQ ID NO:1, Sequence ID No. 2SEQ ID NO:2, Sequence ID No. 22, Sequence ID No. 23~~ and a sequence completely complementary to any of these sequences.

8. (Original) The nucleic acid of claim 7, wherein said sequence is used as a probe or a primer.

9. (Previously presented) A recombinant vector comprising the isolated nucleic acid of claim 1.

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10. (Currently amended) A An isolated host cell comprising the recombinant vector of claim 9.
11. (Withdrawn) A substantially pure mammalian Ese1 or Ese1L protein.
12. (Withdrawn) A substantially pure murine Ese1 or Ese1L protein.
13. (Withdrawn) A substantially pure human Ese1 or Ese1L protein.
14. (Withdrawn) The protein of claim 11 wherein the protein comprises an Ese1 protein comprising the amino acid sequence of Sequence ID No. 3 or the Ese1L protein comprising the amino acid sequence of Sequence ID No. 24.
15. (Withdrawn) A substantially pure polypeptide comprising an amino acid sequence of at least 5 consecutive amino acid residues of Sequence ID No. 3 or Sequence ID No. 24.
16. (Withdrawn) A substantially pure polypeptide comprising at least one functional domain of a mammalian Ese1 protein or a mammalian Ese1L protein.
17. (Withdrawn) A substantially pure polypeptide comprising an antigenic determinant of a mammalian Ese1 protein or a mammalian Ese1L protein.
18. (Withdrawn) An antibody which binds specifically to a polypeptide of claim 16.
19. (Currently amended) A process for recombinantly producing ~~murine Ese1~~ a protein comprising culturing a an isolated host cell comprising a recombinant vector

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comprising the nucleic acid of claim 21 under conditions whereby the ~~Ese1~~ encoded protein is expressed and isolating the ~~Ese1~~ expressed protein therefrom.

20. (Withdrawn) An isolated nucleic acid comprising a nucleotide sequence encoding a mammalian Ese2 protein or a splice variant thereof.
21. (Withdrawn) The nucleic acid of claim 20, wherein said nucleotide sequence encodes a murine Ese2 protein or a splice variant thereof.
22. (Withdrawn) The nucleic acid of claim 20, wherein said nucleotide sequence encodes a human Ese2 protein or a splice variant thereof.
23. (Withdrawn) The nucleic acid sequence of claim 20, wherein said nucleic acid comprises a nucleotide sequence selected from the group consisting of a genomic sequence, a cDNA sequence, a polydeoxyribonucleic acid nucleotide sequence, a polyribonucleic acid nucleotide sequence, an allelic variant or homologue thereof.
24. (Withdrawn) The nucleic acid of claim 20 encoding a protein comprising the amino acid sequence of Sequence ID No. 6 or Sequence ID No. 27.
25. (Withdrawn) The nucleic acid of claim 20 comprising the sequence of Sequence ID No. 4, Sequence ID No. 5, Sequence ID No. 25 or Sequence ID No. 26.
26. (Withdrawn) An isolated nucleic acid comprising a nucleotide sequence of at least 10 consecutive nucleotides selected from the group consisting of Sequence ID No. 4, Sequence ID No. 5, Sequence ID No. 25, Sequence ID No. 26 and a sequence complementary to any of these sequences.

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27. (Withdrawn) The nucleic acid of claim 26, wherein said sequence is used as a probe or a primer.
28. (Withdrawn) A recombinant vector comprising the isolated nucleic acid of claim 20.
29. (Withdrawn) A host cell comprising the recombinant vector of claim 28.
30. (Withdrawn) A substantially pure mammalian Ese2 or Ese2L protein.
31. (Withdrawn) A substantially pure murine Ese2 or Ese2L protein.
32. (Withdrawn) A substantially pure human Ese2 or Ese2L protein.
33. (Withdrawn) The protein of claim 32 wherein the protein comprises an Ese2 protein comprising the amino acid sequence of Sequence ID No. 6 or the Ese2L protein comprising the amino acid sequence of Sequence ID No. 27.
34. (Withdrawn) A substantially pure polypeptide comprising an amino acid sequence of at least 5 consecutive amino acid residues of Sequence ID No. 6 or Sequence ID No. 27.
35. (Withdrawn) A substantially pure polypeptide comprising at least one functional domain of a mammalian Ese2 protein or a mammalian Ese2L protein.
36. (Withdrawn) A substantially pure polypeptide comprising an antigenic determinant of a mammalian Ese2 protein or a mammalian Ese2L protein.

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37. (Withdrawn) An antibody which binds specifically to a polypeptide of claim 36.

38. (Withdrawn) A process for recombinantly producing murine Ese2 protein comprising culturing a host cell comprising a recombinant vector comprising the nucleic acid of claim 20 under conditions whereby the Ese2 protein is expressed and isolating the Ese2 protein therefrom.

39. (Withdrawn) A pharmaceutical composition for the treatment of mammalian disorders which involve abnormal endocytosis leading to altered cellular functioning, said composition comprising an active ingredient selected from the group consisting of;

- a) an Ese protein selected from the group consisting of Ese1, Ese1L, Ese2, Ese2L,
- b) a fragment or mimetic thereof or a non-functional mutant protein, fragment or mimetic thereof of the proteins of a); and
- c) a pharmaceutically acceptable carrier.

40. (Withdrawn) A method of screening a candidate compound for efficacy in treating a disorder characterized by an abnormality in the endocytotic pathway, wherein said pathway involves an interaction between an Ese1, Ese1L, Ese2 or Ese2L protein and a binding partner of any one of these proteins, comprising screening said candidate compound for its ability to disrupt or promote said interaction as an indication of its efficacy.

41. (Withdrawn) A method for preventing or treating a disorder in a mammal characterized by an abnormality in the endocytotic pathway, wherein said pathway involves an interaction between an Ese1, Ese1L, Ese2 or Ese2L protein and a binding

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partner of any one of these proteins, comprising the step of disrupting or promoting said interaction *in vivo*.

42. (Withdrawn) The method of claim 40, wherein said disorder is selected from the group consisting of cancer, abnormal cell division, abnormal cell migration, viral infection, abnormal receptor signalling, abnormal tissue development and abnormal synaptic transmission disorders.

43. (Withdrawn) A method for screening a candidate compound for effectiveness as an antagonist of an Ese protein selected from the group consisting of Ese1, Ese1L, Ese2 and Ese2L, said method comprising:

- (a) providing an assay method for determining the endocytotic regulatory capacity of a selected Ese protein; and
- (b) determining the endocytotic regulatory capacity of the selected Ese protein in the presence or absence of the candidate compound, wherein a reduced level of endocytotic regulatory capacity in the presence of the candidate compound indicates effectiveness of the compound as an antagonist.

44. (Withdrawn) A method for treating in a mammal a disorder associated with an undesired level of endocytotic activity of an Ese protein selected from the group consisting of Ese1, Ese1L, Ese2 and Ese2L, said method comprising administering to the mammal an effective amount of a substance selected from the group consisting of:

- (a) an Ese protein antagonist;
- (b) an antibody which binds specifically to an Ese protein;
- (c) an antisense strand comprising a nucleic acid sequence complementary to a sequence or fragment of the sequence represented by Sequence ID Nos. 1, 2, 4, 5, 22, 23, 25 and 26 and capable of hybridizing to the nucleic acid sequence encoding an Ese protein;

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- (d) an agent which down regulates the expression of an Ese gene encoding for an Ese protein;
- (e) an antagonist of an Ese protein binding partner; and
- (f) an Ese agonist.

45. (Withdrawn) A method for suppressing in a mammal, abnormal proliferation of a cell capable of being stimulated to proliferate by a growth factor receptor, the method comprising administering to the mammal an effective amount of a Ese protein antagonist, an Ese agonist or an antibody which binds specifically to an Ese protein, wherein the Ese protein is selected from the group consisting of Ese1, Ese1L, Ese2 and Ese2L.

46. (Withdrawn) A method for preventing viral infection in a mammal, said method comprising administering to the mammal an effective amount of an Ese protein antagonist, an Ese agonist or an antibody which binds specifically to an Ese protein or an Ese mutant protein not capable of regulating endocytosis, wherein the Ese protein is selected from the group consisting of Ese1, Ese1L, Ese2 and Ese2L.

47. (Withdrawn) A method for promoting endocytosis in selected cells in a mammal in need of such treatment, said method comprising administering to the mammal an effective amount of an Ese protein or an active analogue, mimic or fragment thereof, wherein the Ese protein is selected from the group consisting of Ese1, Ese1L, Ese2 and Ese2L.

48. (Withdrawn) A method for blocking clathrin-mediated endocytosis in cultured cells or in selected cells in a mammal in need of such treatment, said method comprising overexpressing Ese1 protein or an active analogue, mimic or fragment thereof in said cells.

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49. (Withdrawn) A method for regulating endocytosis in cultured cells or in selected cells in a mammal in need of such treatment, said method comprising providing an Ese1-Esp15 complex and further binding dynamin to said complex to regulate components of the endocytic pathway.

50. (Previously presented) A recombinant vector comprising the isolated nucleic acid of claim 7.

51. (Currently amended) ~~A~~An isolated host cell comprising the recombinant vector of claim 50.

52-53. (Canceled)

54. (Withdrawn) A recombinant vector comprising the isolated nucleic acid of claim 26.

55. (Withdrawn) A host cell comprising the recombinant vector of claim 54.

56. (Withdrawn) A process for recombinantly producing murine Ese2 protein comprising culturing a host cell comprising a recombinant vector comprising the nucleic acid of claim 21 under conditions whereby the Ese2 protein is expressed and isolating the Ese2 protein therefrom.

57. (Withdrawn) A process for recombinantly producing murine Ese2 protein comprising culturing a host cell comprising a recombinant vector comprising the nucleic acid of claim 22 under conditions whereby the Ese2 protein is expressed and isolating the Ese2 protein therefrom.

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58. (Withdrawn) The method of claim 41, wherein said disorder is selected from the group consisting of cancer, abnormal cell division, abnormal cell migration, viral infection, abnormal receptor signalling, abnormal tissue development and abnormal synaptic transmission disorders.

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AMENDMENTS TO THE SEQUENCE LISTING AND TO THE SPECIFICATION  
TO ENTER A SUBSTITUTE SEQUENCE LISTING

Please amend the specification by including the enclosed substitute Sequence Listing at the end of the specification. This substitute Sequence Listing is to replace all prior Sequence Listings. The enclosed substitute Sequence Listing has been amended to add the *Xenopus* and *Drosophila* amino acid sequences of Figure 2B as SEQ ID NOS:34 and 35, respectively, thereby permitting proper identification of these sequences. Also enclosed is a computer readable form of the enclosed substitute Sequence Listing.

Applicants assert that the content of the paper copy and computer readable form of the Sequence Listing, submitted concurrently herewith in accordance with 37 CFR§ 1.821(c) and (e), is the same. Applicants also assert, as required under 37 CFR § 1.821(h), that the paper and computer readable forms contain no new matter, nor do they go beyond the disclosure of the application as filed.